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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/911,569	07/23/2001	Pamela Hawley-Nelson	32-95D	8436

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GREENLEE WINNER AND SULLIVAN P C
4875 PEARL EAST CIRCLE
SUITE 200
BOULDER, CO 80301

EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 07/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/911,569	HAWLEY-NELSON ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,10-14,17,18,20,27-36,38-41,51-54,78-83,86-88 and 94-129* is/are pending in the application.

4a) Of the above claim(s) *10,11,100 and 101* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,12-14,17,18,20,27-36,38-41,51-54,78-83,86-88,94-99 and 102-129* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/17/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the amendment, filed 4/21/2005, in which claims 1-6, 8, 9, 15, 16, 19, 21-26, 37, 42-50, 55-77, 84, 85 and 89-93 were canceled; claims 7, 10-14, 17, 18, 20, 27, 29-36, 38-41, 51, 54, 78-83, 86 and 87 were amended; and claims 94-129 were newly added. Claims 7, 10-14, 17, 18, 20, 27-36, 38-41, 51-54, 78-83, 86-88 and 94-129 are pending in the instant application. Claims 7, 12-14, 17, 18, 20, 27-36, 38-41, 51-54, 78-83, 86-88, 94-99 and 102-129 are currently under consideration. Claims 10, 11, 100 and 101 are withdrawn from consideration as being drawn to a non-elected invention.

Any rejection of record in the previous office actions not addressed herein is withdrawn. New grounds of rejection are presented herein that were not necessitated by applicant's amendment of the claims since the office action mailed 10/21/2004. Therefore, this action is not final.

Claim Objections

Claims 13, 20, 29, 31, 104, 110 and 112 are objected to because of the following informalities: the claims read on a non-elected invention.

Claim 96 is objected to because of the following informalities: the term "nucleic acid molecules" is misspelled. Appropriate correction is required.

Terminal Disclaimer

The terminal disclaimers filed on 4/21/2005 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration dates of US Patent

No. 6,051,429 and US Patent No. 6,376,248 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7, 12, 14, 17, 18, 32-36, 39, 40, 41, 51, 52, 54, 78-83, 86, 88, 94-99, 106 and 114-129 are rejected under 35 U.S.C. 102(b) as being anticipated by Whittaker et al (WO 96/05218, cited in a prior action; see the entire reference). **This is a new rejection.**

Regarding claim 17, Whittaker et al teach a cell transfection composition comprising a peptide covalently attached to a lipid, wherein the peptide-lipid compound is non-covalently associated with a nucleic acid molecule (e.g. pages 1, line 1, to page 3, line 15). The peptide may be covalently attached through a linker, which may consist of a polymer of lysine (e.g. page 4, lines 7-12; page 1, lines 25-35). The addition of positively charged amino acids to the lipid will render it a cationic lipid.

Regarding claims 7, 14 and 88, Whittaker et al teach the composition further comprising neutral lipid such as dioleoyl phosphatidyl ethanolamine (DOPE) or cholesterol, for example (e.g. paragraph bridging pages 4-5).

Regarding claim 12, Whittaker teach the composition with an addition of more than one charged amino acid, such as lysine, to the linker, and thus teach a polyvalent cationic lipid (e.g. page 4, lines 7-12 and 25-30).

Regarding claim 36, Whittaker et al teach the composition comprising a peptide that includes a nucleic acid binding domain in tandem (i.e. a multimer) with another peptide sequence or on a bifurcating structure (e.g. paragraph bridging pages 3 and 4).

Regarding claim 39, Whittaker et al teach a mixture of pGFP-N1 plasmid and K3ATL3 in 5% dextrose in water, which was injected into mice (e.g. page 40, lines 20-26). Thus, Whittaker et al necessarily teach the transfection composition further comprising a pharmaceutical carrier.

Regarding claim 40, Whittaker et al teach the compositions comprising therapeutic nucleic acids (e.g. page 5, lines 12-18).

Regarding claim 41, Whittaker et al teach the composition comprising the CAT gene which can be used to diagnose cells for gene expression and transfection efficiency (e.g. paragraph bridging pages 17-18).

Regarding claim 78, Whittaker et al teach the composition comprising DNA molecules (e.g. page 3, lines 14-25).

Regarding claim 79, Whittaker et al teach the composition comprising RNA molecules (e.g. page 3, lines 14-25).

Regarding claim 80, Whittaker et al teach the composition comprising ribozymes and antisense molecules (e.g. paragraph bridging pages 40-41).

Regarding claim 81, Whittaker et al teach the composition comprising the CAT gene which can be used to diagnose cells for gene expression and transfection efficiency (e.g. paragraph bridging pages 17-18).

Regarding claim 82, Whittaker et al teach the use the composition comprising therapeutic nucleic acids (e.g. page 5, lines 12-18).

Regarding claim 83, Whittaker et al teach the composition comprising natural bases, non-natural bases, nucleic acids that express proteins, and nucleic acids that inhibit protein expression (e.g. page 3, lines 14-18; paragraph bridging pages 17-18; paragraph bridging pages 40-41).

Regarding claim 86, Whittaker et al teach that the peptide of the composition may be covalently attached through a linker, which may consist of a polymer of lysine (e.g. page 4, lines 7-12; page 1, lines 25-35). The lysine residues comprise ammonium groups, and thus the lipids are polycationic ammonium lipids.

Regarding claim 94, Whittaker et al teach the composition comprising a peptide with a nuclear localization signal sequence (e.g. paragraph bridging pages 3-4).

Regarding claims 95-97, a kit can be defined as a set of articles or implements used for a specific purpose (e.g. *The American Heritage® Dictionary of the English Language, Fourth Edition, Copyright © 2000 by Houghton Mifflin Company*). Thus, Whittaker et al teach a kit comprising a transfection reagent comprising a peptide covalently attached to a lipid, wherein the peptide-lipid compound is non-covalently associated with a nucleic acid molecule (e.g. pages 1, line 1, to page 3, line 15). Further, Whittaker et al teach the composition comprising the CAT gene which can be used to diagnose cells for gene expression and transfection efficiency (e.g. paragraph bridging pages 17-18).

Regarding claim 52, Whittaker et al teach a method comprising contacting the composition with a cell (e.g. page 3, lines 18-25; page 17, lines 30-35).

Regarding claim 32, Whittaker et al teach the use of established cell lines or primary cell lines (e.g. page 3, lines 18-25).

Regarding claim 33 and 34, Whittaker et al teach the use of human cell lines such as PC3 and Jurkat cells (e.g. Figure 22).

Regarding claim 35, Whittaker et al incorporate by reference EP0424688, which teaches the transfection of fibroblast cells (e.g. page 4, lines 5-16; page 6, lines 30-50).

Regarding claim 18, Whittaker et al teach a cell transfection composition comprising a peptide covalently attached to a lipid, wherein the peptide-lipid compound is non-covalently associated with a nucleic acid molecule (e.g. pages 1, line 1, to page 3, line 15). The peptide may be covalently attached without a linker to a neutral lipid (e.g. pages 1, line 1, to page 3, line 15). Further, Whittaker et al teach the formulation of the composition into liposomes by standard methods with a lipid such as DOPC, a monovalent cationic lipid (e.g. paragraph bridging pages 4-5).

Regarding claims 98 and 99, Whittaker et al teach the composition further comprising cholesterol (e.g. paragraph bridging pages 4-5).

Regarding claim 106, Whittaker et al teach the composition comprising a peptide with a nuclear localization signal sequence (e.g. paragraph bridging pages 3-4).

Regarding claim 114, Whittaker et al teach the composition comprising DNA molecules (e.g. page 3, lines 14-25).

Regarding claim 115, Whittaker et al teach the composition comprising RNA molecules (e.g. page 3, lines 14-25).

Regarding claim 116, Whittaker et al teach the composition comprising ribozymes and antisense molecules (e.g. paragraph bridging pages 40-41).

Regarding claim 117, Whittaker et al teach the composition comprising the CAT gene which can be used to diagnose cells for gene expression and transfection efficiency (e.g. paragraph bridging pages 17-18).

Regarding claim 118, Whittaker et al teach the use the composition comprising therapeutic nucleic acids (e.g. page 5, lines 12-18).

Regarding claim 119, Whittaker et al teach the composition comprising natural bases, non-natural bases, nucleic acids that express proteins, and nucleic acids that inhibit protein expression (e.g. page 3, lines 14-18; paragraph bridging pages 17-18; paragraph bridging pages 40-41).

Regarding claim 124, Whittaker et al teach a mixture of pGFP-N1 plasmid and K3ATL3 in 5% dextrose in water, which was injected into mice (e.g. page 40, lines 20-26). Thus, Whittaker et al necessarily teach the transfection composition further comprising a pharmaceutical carrier.

Regarding claim 125, Whittaker et al teach the compositions comprising therapeutic nucleic acids (e.g. page 5, lines 12-18).

Regarding claim 126, Whittaker et al teach the composition comprising the CAT gene which can be used to diagnose cells for gene expression and transfection efficiency (e.g. paragraph bridging pages 17-18).

Regarding claims 127-129, a kit can be defined as a set of articles or implements used for a specific purpose (e.g. *The American Heritage® Dictionary of the English Language, Fourth Edition, Copyright © 2000 by Houghton Mifflin Company*). Thus, Whittaker et al teach a kit comprising a transfection reagent comprising a peptide covalently attached to a lipid, wherein the peptide-lipid compound is non-covalently associated with a nucleic acid molecule (e.g. pages 1, line 1, to page 3, line 15). Further, Whittaker et al teach the composition comprising the CAT gene which can be used to diagnose cells for gene expression and transfection efficiency (e.g. paragraph bridging pages 17-18).

Regarding claims 51 and 54, Whittaker et al teach a method comprising contacting the composition with a cell (e.g. page 3, lines 18-25; page 17, lines 30-35).

Regarding claim 120, Whittaker et al teach the use of established cell lines or primary cell lines (e.g. page 3, lines 18-25).

Regarding claims 121 and 122, Whittaker et al teach the use of human cell lines such as PC3 and Jurkat cells (e.g. Figure 22).

Regarding claim 123, Whittaker et al incorporate by reference EP0424688, which teaches the transfection of fibroblast cells (e.g. page 4, lines 5-16; page 6, lines 30-50).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7, 12-14, 17, 18, 32-36, 39, 40, 41, 51, 52, 54, 78-83, 86-88, 94-99, 102-106 and 114-129 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whittaker et al (WO 96/05218, cited in a prior action; see the entire reference) in view of Haces et al (US Patent No. 5,674,908, cited in a prior action; see the entire reference). **This is a new rejection.**

The teachings of Whittaker et al are described above and applied as before. Further, Whittaker et al teach it is within the skill of the art to formulate the composition comprising a lipid covalently linked to a peptide into liposomes containing a cationic or neutral lipid (e.g. paragraph bridging pages 4-5). Moreover, Whittaker et al teach that combinations of lipopeptide reagents can achieve superior levels of transfection compared to single agent s alone (e.g. page 40, lines 9-15).

Whittaker et al do not teach compositions comprising DOSPA.

Haces et al disclose highly packed polycationic ammonium lipid compounds useful for making lipid aggregates for delivery of macromolecules into cells (e.g. Abstract; column 3, formula I). Further, Haces et al teach that the compounds are useful alone or in combination

with other lipid aggregate-forming components such as DOSPA and DOPE (e.g. column 4, lines 51-59). Moreover, Haces et al teach that the compounds are superior intracellular delivery agents and are less toxic to the target cells (e.g. column 5, lines 17-20).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition and method of using said composition of Whittaker et al to include the lipids taught by Haces et al because Whittaker et al and Haces et al teach it is within the ordinary skill in the art to use different combinations of lipids as compositions for the transfection of cells.

One would have been motivated to make such a modification in order to receive the expected benefit of superior intracellular delivery and reduced toxicity as taught by Haces et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 7, 12, 14, 17, 18, 20, 27-29, 31-36, 38, 39, 40, 41, 51, 52-54, 78-83, 86, 88, 94-99, 106-110 and 112-129 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whittaker et al (WO 96/05218, cited in a prior action; see the entire reference) in view of O'Hare et al (WO 97/05265, cited in a prior action; see the entire reference). **This is a new rejection.**

The teachings of Whittaker et al are described above and applied as before.

Whittaker et al do not teach compositions comprising herpes simplex VP22 protein.

O'Hare et al teach methods of transfecting a population of cells by contacting cells with a composition comprising a lipid vesicle, nucleic acid and a transport protein (e.g. page 5, lines 18-

24; page 6, lines 28-34; page 18, lines). Further, O'Hare et al teach the use of the herpes simplex virus VP22 protein, or fragments thereof, as the transport protein with the ability to localize to the nucleus (e.g. page 4, lines 18-33; Figure 1). Moreover, O'Hare et al demonstrate the rapid and efficient uptake of VP22 protein from the cell culture medium (e.g. page 15, lines 15-28).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the transfection composition and method of using said composition of Whittaker et al to include the VP22 protein taught by O'Hare et al because Whittaker et al and O'Hare et al teach the use of compositions comprising lipid and protein to transfect cells.

One would have been motivated to make such a modification in order to receive the expected benefit of more efficient and rapid transfection and nuclear localization as taught by O'Hare et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 7, 12, 14, 17, 18, 30, 32-36, 39, 40, 41, 51, 52, 54, 78-83, 86-88, 94-99, 105, 106, 111 and 114-129 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whittaker et al (WO 96/05218, cited in a prior action; see the entire reference) in view of Felgner et al (The Journal of Biological Chemistry, Vol. 269, No. 4, pages 2550-2561, 1994; see the entire reference). **This is a new rejection.**

The teachings of Whittaker et al are described above and applied as before.

Whittaker et al do not teach the addition of chloroquine to the transfection compositions or the addition of cationic lipids that comprise saturated and unsaturated alkyl and alicyclic ethers and esters of amines, amides or derivatives thereof.

Felgner et al teach the additions of chloroquine to transfection compositions comprising lipids such as DOPE, lysoOPE, and DOTMA, for example (e.g. Abstract; page 2551, Materials, Chemistry, Preparation of Cationic Liposome Formulations; Figure 1; Figure 2). Further, Felgner et al teach that chloroquine can enhance the transfection efficiency of liposome-mediated transfection methods (e.g. paragraph bridging pages 2560-2561).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the transfection compositions of Whittaker et al to include the lipids and chloroquine taught by Felgner et al because Whittaker et al and Felgner et al teach it is within the ordinary skill in the art to use lipid-containing compositions for the transfection of cells.

One would have been motivated to make such a modification in order to receive the expected benefit of enhanced transfection efficiency as taught by Felgner et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR, http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jennifer Dunston
Examiner
Art Unit 1636

jad

TERRY MCKELVEY
PRIMARY EXAMINER